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**NOTICE OF ALLOWANCE
AND ISSUE FEE DUE**

☐ Note attached communication from the Examiner

☐ This notice is issued in view of applicant's communication filed

SERIES CODE/SERIAL NO.	FILING DATE	TOTAL CLAIMS	EXAMINER AND GROUP ART UNIT	DATE MAILED
08/217,921	03/25/94	007	STANTON, B	1819 11/26/96
First Named Applicant	HOGAN,	BRIGID L.M.		

TITLE OF INVENTION: PLURIPOTENTIAL EMBRYONIC STEM CELLS AND METHODS OF MAKING SAME

	ATTY'S DOCKET NO.	CLASS-SUBCLASS	BATCH NO.	APPLN. TYPE	SMALL ENTITY	FEE DUE	DATE DUE
1	1616.002	424-093.100	689	UTILITY	YES	\$645.00	02/26/97

**THE APPLICATION IDENTIFIES ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT.
PROSECUTION ON THE MERITS IS CLOSED.**

**THE ISSUE FEE MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS
APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED.**

HOW TO RESPOND TO THIS NOTICE:

I. Review the SMALL ENTITY Status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

- A. If the status is changed, pay twice the amount of the FEE DUE shown above and notify the patent and Trademark Office of the change in status, or
- B. If the Status is the same, pay the FEE DUE shown above.

If the SMALL ENTITY is shown as NO:

- A. Pay FEE DUE shown above, or
- B. File verified statement of Small Entity Status before, or with, pay of 1/2 the FEE DUE shown above.

II. Part B of this notice should be completed and returned to the Patent and Trademark Office (PTO) with your ISSUE FEE. Even if the ISSUE FEE has already been paid by charge to deposit account, Part B should be completed and returned. If you are charging the ISSUE FEE to your deposit account, Part C of this notice should also be completed and returned.

III. All communications regarding this application must give series code (or filing date), serial number and batch number. Please direct all communication prior to issuance to Box ISSUE FEE unless advised to contrary.

IMPORTANT REMINDER: Patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

Notice of Allowability

Application No.
08/217,921

Applicant(s)
Hogan

Examiner
Brian R. Stanton

Group Art Unit
1819



All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance and Issue Fee Due or other appropriate communication will be mailed in due course.

☒ This communication is responsive to 8/29/96

☒ The allowed claim(s) is/are 1-4, 7, 30, and 31

☐ The drawings filed on _____ are acceptable.

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

A SHORTENED STATUTORY PERIOD FOR RESPONSE to comply with the requirements noted below is set to EXPIRE **THREE MONTHS** FROM THE "DATE MAILED" of this Office action. Failure to timely comply will result in ABANDONMENT of this application. Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

☐ Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL APPLICATION, PTO-152, which discloses that the oath or declaration is deficient. A SUBSTITUTE OATH OR DECLARATION IS REQUIRED.

☒ Applicant MUST submit NEW FORMAL DRAWINGS

☐ because the originally filed drawings were declared by applicant to be informal.

☒ including changes required by the Notice of Draftsperson's Patent Drawing Review, PTO-948, attached hereto or to Paper No. 7

☐ including changes required by the proposed drawing correction filed on _____, which has been approved by the examiner.

☐ including changes required by the attached Examiner's Amendment/Comment.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the reverse side of the drawings. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

☐ Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Any response to this letter should include, in the upper right hand corner, the APPLICATION NUMBER (SERIES CODE/SERIAL NUMBER). If applicant has received a Notice of Allowance and Issue Fee Due, the ISSUE BATCH NUMBER and DATE of the NOTICE OF ALLOWANCE should also be included.

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

☒ Interview Summary, PTO-413

☒ Examiner's Amendment/Comment

☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material

☒ Examiner's Statement of Reasons for Allowance

BRIAN R. STANTON
PRIMARY EXAMINER
GROUP 1800

#14/29

Serial Number: 08/217,921

Art Unit: 1819

The amendments filed on 8/15/96 and 8/29/96 (Papers numbered 11 and 12, respectively) have been entered. Claims 1-4, 7, 30, 31, 33, and 34 remain pending in the instant Application.

An Examiner's Amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 C.F.R. § 1.312. To ensure consideration of such an amendment, it **MUST** be submitted no later than the payment of the Issue Fee.

Authorization for this Examiner's Amendment was given in a telephone interview with David Perryman on 11/20/96.

The application has been amended as follows:

IN THE SPECIFICATION:

On page 1, in the title on line 1, "stem" has been deleted.

The abstract on page 35 has been deleted and the following text inserted therefore:

— The claimed invention is directed towards non-murine pluripotent cells that have the ability to be passaged *in vitro* for at least 20 passages and which differentiate in culture into a variety of tissues. The scope of the claimed cells includes any non-murine ES cells and particular claims are drawn to human pluripotent cells.—

IN THE CLAIMS:

Claims 33 and 34 have been cancelled.

Claim 1 has been rewritten as follows:

1. An isolated non-murine mammalian pluripotent cell wherein said cell exhibits the following characteristics:

- (a) can be maintained on feeder layers for at least 20 passages; and
(b) gives rise to embryoid bodies and differentiated cells of multiple phenotypes in monolayer culture; and wherein said cell is derived from a primordial germ cell by the process of:
- (1) culturing a non-murine mammalian primordial germ cell in a composition comprising ^{basic} ~~basic~~ fibroblast growth factor, leukemia inhibitory factor, membrane associated steel factor, and soluble steel factor;
 - (2) selecting cells that have characteristics (a) and (b), above, and
 - (3) isolating said non-murine pluripotent cell.

Claims 2 and 3 have been amended as follows:

In claim 2, on line 1, "stem" has been deleted and ---pluripotent--- inserted therefor.

In claim 3, on line 1, "stem" has been deleted and ---pluripotent--- inserted therefor.

Claims 4, 7, 30, and 31, have been rewritten as follows:

6. An isolated human pluripotent cell wherein said cell exhibits the following characteristics:

- (a) can be maintained on feeder layers for at least 20 passages; and
(b) gives rise to embryoid bodies and differentiated cells of multiple phenotypes in monolayer culture; and wherein said cell is derived from a human primordial germ cell by the process of:
- (1) culturing a human primordial germ cell in a composition comprising ^{basic} ~~basic~~ fibroblast growth factor, leukemia inhibitory factor, membrane associated steel factor, and soluble steel factor;
 - (2) selecting cells that have characteristics (a) and (b), above, and
 - (3) isolating said human pluripotent cell.

7. A composition comprising:

- (A) a human pluripotent cell derived from a primordial germ cell wherein said cell exhibits the following characteristics:
- (1) can be maintained on feeder layers for at least 20 passages; and
 - (2) gives rise to embryoid bodies and differentiated cells of multiple phenotypes in monolayer culture; and wherein said cell is derived from a primordial germ cell by the process of:
 - (a) culturing a human primordial germ cell in a composition comprising ^{basic} ~~basic~~ fibroblast growth factor, leukemia inhibitory factor, membrane associated steel factor, and soluble steel factor;
 - (b) selecting cells that have characteristics (a) and (b), above, and
 - (c) isolating said human pluripotent cell; and
- (B) a fibroblast growth factor, leukemia inhibitory factor, membrane associated steel factor, and soluble steel factor, each in amounts sufficient to permit continued proliferation of said cell.

D4 E
A 30

A method of using a non-murine and non-human pluripotent cell of claim 1 to contribute to chimeras *in vivo* comprising:

- injecting the cell into a blastocyst of the same species of said cell;
- implanting the resultant chimeric blastocyst into a foster mother of the same species; and
- allowing the chimeric blastocyst to grow within the foster mother.

D5 5
31

A method of using a non-murine and non-human pluripotent cell of claim 1 to contribute to chimeras *in vivo* comprising:

- aggregating the cell with a morula stage embryo of the same species of said cell;
- implanting the resultant chimeric embryo into a foster mother of the same species; and
- allowing the chimeric embryo to grow within the foster mother.

The following is an Examiner's Statement of Reasons for Allowance:

The claimed invention is drawn to non-murine compositions of pluripotential cells that are prepared from primordial germ cells. While the prior art as represented by e.g., Matsui et al., 1992 (AA1) indicated that one could have prepared embryonic stem cells from murine primordial germ cells, the state of the art at the time of the invention indicates that one would not have had a reasonable expectation of success in preparing either embryonic stem or other pluripotential cells from primordial germ cells of other species. However, once the claimed compositions and methods were practiced in divergent mammalian species such as mouse and human, as instantly disclosed, one would have had a reasonable expectation of being able to have practiced the claimed methods in a variety of mammalian systems. Therefore, the claimed invention is found to meet the collective requirements for patentability.

Any comments considered necessary by applicant must be submitted no later than the payment of the Issue Fee and, to avoid processing delays, should preferably accompany the Issue Fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Papers related to this application may be submitted to the Group 1800 by facsimile transmission. Papers should be faxed to the Group 1800 via the PTO FAX center located in Crystal Mall I. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG (30 November 1989). The CM1 Fax Center Number is (703) 308-0294.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian R. Stanton whose telephone number is (703) 308-2801. The examiner can normally be reached on Monday through Thursday from 6:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jasmine Chambers can be reached on (703) 308-2035.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1096.



Brian R. Stanton, Ph.D.
November 21, 1996

**BRIAN R. STANTON
PRIMARY EXAMINER
GROUP 1800**

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